

REMARKS

Claims 1-30 are pending in the present application. Claims 2, and 11-27, were subject to restriction and have been withdrawn from consideration. Therefore, claims 1, and 3-10, remain under examination in the present application. Additionally, claims 28-30 are newly added.

Claims 1, 3 and 8-10, have been amended to replace the term "crude Dunaliella powder" with the term "dried Dunaliella algae." Support for this amendment appears in the specification at page 6, line 27. In addition, claim 1 has been amended to correct a minor grammatical error. Each amended claim and its corresponding original claim, are of equivalent scope. No new matter has been added.

Claims 5-7 and 9 have been amended to comply with United States claim form. Each amended claim and its corresponding original claim are of equivalent scope. Claims 5-7 have been amended to place them in proper Markush form. Claim 9 has been amended as suggested by the Examiner. No new matter has been added.

Claim 2 has been amended to correct a minor typographical error. More specifically "HLD" has been replaced by "HDL."

Newly added claim 28 recites that the dried Dunaliella algae comprises β -carotene. Support for this amendment appears in the specification at page 1, last line; page 2, lines 1-5; page 8, lines 22-23; and Example VI at page 11. No new matter has been added.

Newly added claims 29 and 30 recite that the β-carotene comprises “9-cis β-carotene” and “an approximately 1:1 ratio of all-trans β-carotene and 9-cis β-carotene” respectively. Support for newly added claims 29 and 30 can be found in the specification at, for example, page 2, lines 1-2, and page 8, lines 23-29.

In view of the remarks set forth below, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, claims 1, and 3-10, have been rejected under 35 USC § 112, second paragraph as being indefinite.

The Examiner asserts that the term “crude Dunaliella powder,” recited in claims 1 and 9, is unclear and renders the claims vague and ambiguous.

Claims 1, 3 and 8-10, have been amended to replace the term “crude Dunaliella powder” with the term “dried Dunaliella algae.” The specification at page 6, lines 26-27, recites that the active ingredient of the crude preparation is dried Dunaliella algae. See also page 8, lines 21-28.

It is submitted that claims 1 and 3-10 are clear and definite within the meaning of 35 USC § 112, second paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

II. At page 3 of the Official Action, claims 1, 8, and 9, are rejected under 35 USC § 102(a) as being anticipated by Japanese Patent 2003180387 (Hayashi).

In view of the following, this rejection is moot.

Applicants submit that Hayashi does not constitute prior art against the present application because Applicants' date of invention of the presently

claimed subject matter occurred prior to the publication date of the Hayashi reference. According to 37 CFR § 1.31 (b) in a declaration of prior invention:

[t]he showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application. Original exhibits of drawings or records, or photocopies thereof, must accompany and form part of the affidavit or declaration or their absence must be satisfactorily explained. See MPEP § 715.

Submitted herewith is a Declaration under 37 CFR § 1.131 executed by the present inventors, along with supporting documentation (Exhibits A through D), evidencing that Applicants' date of invention occurred prior to the July 2, 2003 effective date of the Hayashi reference.

As shown by the attached dated Experimental Protocol (Exhibit A), the inventors studied the effect of Dunaliella on mice. The Experimental Protocol, Exhibit A, describes: separating the mice into a first group of mice (the control group) and a second group of mice (the experimental group); after three weeks inducing diabetes in the mice by administering STZ over a five day period; following another three weeks, administering Dunaliella to the experimental group of mice; and periodically testing the mice for blood plasma levels of glucose, insulin, cholesterol, and triglycerides.

From the Experimental Protocol, it can be seen the mice were first bled on May 5, 2003, at which time their blood glucose plasma levels were tested and recorded. The second bleeding occurred on May 29, 2003. STZ was administered to the mice over a five day period of beginning on June 1, 2003.

Diabetes was thereby induced, as evidenced by the blood glucose plasma levels recorded on June 22, 2004. The third bleeding occurred on June 26, 2003. The mice were last bled on July 16, 2003.

As Evidenced by the data gathered from the subject experiment (Exhibit C), it is clear that blood glucose levels were reduced in the Experimental group. Thus, it is evident that the claimed subject matter was invented, within the meaning of 37 USC § 1.131, prior to the July 2, 2006 effective date of the Hayashi reference. Accordingly, this rejection is moot.

With regard to newly added claims 28-30, claim 28 recites that the dried Dunaliella algae comprises β -carotene. Claim 29 and 30 depend from claim 28. Assuming *arguendo* that Hayashi constitutes prior art against the present application, it is submitted that Hayashi does not teach each and every element of the claimed invention.

Hayashi describes orally administering Dunaliella containing only non-cyclic carotenoids, i.e., phytoene. Hayashi describes in paragraph [0005] that specific culture medium containing nicotine is used in order to manufacture "simply the carotenoid containing the phytoene which are non-ring type carotenoids other than the carotenoid manufactured by culture of the conventional Dunaliella frond." See also paragraph [0031].

Nicotine is a cyclase inhibitor known to induce the accumulation of β -carotene intermediates including phytoene and lycopene and inhibit the production of β -carotene itself in algae. See Shaish, A. et al., Plant Cell Physiol. 31:689 (1990), submitted herewith.

In view of the foregoing, Hayashi does not teach administering to a subject an effective amount of dried Dunaliella algae comprising β -carotene, as claimed in newly added claim 28.

Accordingly, assuming *arguendo* Hayashi constitutes prior art against the present claims, Hayashi does not teach each and every element of claim 28, as required for anticipation under 35 USC § 102 (a). Therefore, claims 29 and 30 are novel as well.

III. At page 4 of the Official Action, claims 1 and 8-10 are rejected under 35 USC § 103(a) as being unpatentable over Hayashi in view of Takenaka et al. and Levy et al.

The Examiner asserts that it would have been obvious to the skilled artisan to modify Hayashi, by encapsulating the Dunaliella powder as taught by Takenaka et al. and Levy et al. to achieve the present invention. In view of the remarks set forth herein, this rejection is respectfully traversed.

In view of the Declaration under 35 USC § 1.131 submitted herewith and the discussion set forth above, Applicants assert that Hayashi does not constitute prior art against the present application because Applicants invented the presently claimed subject matter prior to Hayashi's effective date of July 2, 2003 as evidenced by the declaration. Accordingly, this rejection is moot.

Present claim 1 recites a method for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels. Claims 8-10 are dependent on claim 1.

To establish a *prima facie* case of obviousness, the Examiner must establish: (1) that some suggestion or motivation to modify the references exists; (2) a reasonable expectation of success; and (3) that the prior art references teach or suggest all the claim limitations. *Amgen, Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present invention. See *Ex parte Clapp*, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The Examiner bears the initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. *Id.* at 974.

The court in *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994), held that "A prior art reference may be said to *teach away* when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." The court in *Busch & Lamb, Inc. v. Barnes-Hind/Hydro curve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986), held that "A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered."

As discussed, Applicants respectfully submit that Hayashi is not prior art against the present application. Therefore, a *prima facie* case of obviousness has not been established because Takenaka et al. and Levy et al. fail to teach or

suggest all of the limitations of the claims as required by *Amgen* and *In re Wilson*.

Takenaka does not teach or suggest a method for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels, as recited in the present claims. Rather, Takenaka et al. describes a preparation of a soft capsule for foods made from blending carotenoids extracted from algae with nutrients unstable to light and oxidation.

Likewise, Levy et al. does not cure the deficiencies of Takenaka et al., because Levy et al. does not teach or suggest a method for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels, as recited in the present claims. Rather, Levy et al. describes the use of powdered Dunaliella to reduce the susceptibility to oxidation of LDL.

In view of the above, it is submitted that nothing in Takenaka et al., and Levy et al., taken alone or in combination, renders the invention of claims 1, and 8-10, obvious within the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

With regard to newly added claim 28, claim 28 recites that the dried Dunaliella algae comprises β-carotene. New claims 29 and 30 depend from claim 28. Assuming *arguendo* that Hayashi constitutes prior art against the present application, in view of the following applicants respectfully submit that

new claims 28-30 are also not rendered obvious by Hayashi in view of Takenaka et al. and Levy et al. Further, it is submitted that a *prima facie* case of obviousness has not been established.

A *prima facie* case of obviousness has not been established because Hayashi in view of Takenaka et al. and Levy et al. fail to teach or suggest all of the limitations of the claims as required by *Amgen* and *In re Wilson*. Hayashi does not teach or suggest administering dried Dunaliella algae comprising β-carotene to a subject, as claimed in newly added claim 28.

In fact, Hayashi **teaches away** from administering dried Dunaliella algae comprising β-carotene because Hayashi **expressly** requires culturing Dunaliella algae in a culture medium containing nicotine so that **only non-cyclic carotenoids are produced**. Again, Hayashi describes that only non-cyclic carotenoids “other than the carotenoid manufactured by culture of the conventional Dunaliella frond” are produced. Please see the above discussion of Hayashi

Takenaka et al. does not cure the deficiencies of Hayashi because Takenaka does not teach or suggest a method for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae comprising β-carotene to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels, as recited in the present claims. Rather, Takenaka et al. describes a preparation of a soft capsule for foods made from blending carotenoids extracted from algae with nutrients unstable to light and oxidation.

Likewise, Levy et al. does not cure the deficiencies of Hayashi and/or Takenaka et al., because Levy et al. does not teach or suggest a method for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae comprising β-carotene to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels, as recited in the present claims. Rather, Levy et al. describes the use of powdered Dunaliella to reduce the susceptibility to oxidation of LDL.

In view of the above, assuming *arguendo* that Hayashi constitutes prior art, it is submitted that nothing in Hayashi, Takenaka et al., and Levy et al., taken alone or in combination, renders the invention of claims 28-30 obvious within the meaning of 35 USC § 103.

IV. At page 5 of the Official Action, claims 1 and 3-10 are rejected under 35 USC § 103(a) as being unpatentable over Hayashi, Takenaka et al., and Levy et al., in view of Beck, Pan et al., Heymen et al., and Smith.

The Examiner asserts that it would have been obvious to the skilled artisan to add any of the ingredients taught by Beck, Pan et al., Heyman et al. or Smith with the combined teachings of Hayashi, Takenaka et al., and Levy et al. In view of the remarks set forth herein, this rejection is respectfully traversed.

As previously discussed, Hayashi does not constitute prior art against the present application. Please see the remarks set forth herein with regard to Hayashi and the Declaration under 37 CFR § 1.131 submitted herewith.

Again, as discussed, Applicants respectfully submit that Hayashi is not prior art against the present application. Therefore, a case of *prima facie* obviousness has not been established.

Applicants submit that a *prima facie* case of obviousness has not been established because: (i) there is no suggestion or motivation to modify the combination of Takenaka et al, and Levy et al., by incorporating any of the ingredients of Beck, Pan et al., Heyman et al. or Smith; and (ii) Takenaka et al. and Levy et al. fail to teach or suggest all of the limitations of the claims as required by *Amgen* and *In re Wilson*.

Regarding (i), as Hayashi is not prior art against the presently claimed invention, none of the applied references provide any suggestion or motivation for modifying Dunaliella by adding activators of nuclear receptors to reduce insulin and/or glucose plasma levels in a subject afflicted with diabetes.

With regard to (ii), nothing in any of Takenaka et al., and Levy et al., taken alone or in combination, teach or suggest administering dried Dunaliella algae to a subject, as claimed in present claims 1 and 3-10.

As discussed above, Applicants respectfully submit that Hayashi is not prior art against the present application. Further, Applicants submit that Takenaka et al. and Levy et al., taken alone or in combination, do not render the presently claimed invention obvious within the meaning of 35 USC § 103.

None of Beck, Pan et al., Heyman et al., and Smith, taken alone or in combination, cures the deficiencies of Takenaka et al., and Levy et al., because none of Beck, Pan et al., Heyman et al., and Smith, teach or suggest a method

for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels, as claimed in present claims 1 and 3-10.

Rather, Beck describes the use of bezafibrate for the treatment of normolipidaemic diabetes mellitus type II. Pan et al. describes a method for reducing the risk of Type II diabetes by administering a combination of: (1) a cholesterol lowering drug such as mevastatin, lovastatin, pravastatin or velostatin; and (2) an angiotensin converting enzyme inhibitor. Heyman describes methods and compositions for the treatment of non-insulin-dependent diabetes mellitus using an RXR agonist alone or in combination with a PPAR- γ agonist, e.g. a thiazolidinedione compound. Lastly, Smith describes a method for the treatment of diabetes mellitus comprising administering rosiglitazone and insulin.

In view of the foregoing, it is submitted that nothing in any of the applied references, taken alone or in combination, renders the claimed invention obvious within the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

With regard to newly added claim 28, claim 28 recites that the dried Dunaliella algae comprises β -carotene. Claims 29 and 30 depend from claim 28. Again, assuming *arguendo* that Hayashi constitutes prior art against the present application, applicants respectfully submit that new claims 28-30 are also not rendered obvious by Hayashi, Takenaka et al., and Levy et al., in view of Beck,

Pan et al., Heymen et al., and Smith. Further it is submitted that, a case of *prima facie* obviousness has not been established.

Applicants submit that a *prima facie* case of obviousness has not been established because: (i) there is no suggestion or motivation to modify the combination of Hayashi, Takenaka et al, and Levy et al., by incorporating any of the ingredients of Beck, Pan et al., Heyman et al. or Smith; and (ii) Hayashi in view of Takenaka et al. and Levy et al. fail to teach or suggest all of the limitations of the claims as required by Amgen and *In re Wilson*.

Regarding (i), none of the applied references provide any suggestion or motivation for modifying the Dunaliella of Hayashi by adding activators of nuclear receptors to reduce insulin and/or glucose plasma levels in a subject afflicted with diabetes.

With regard to (ii), nothing in any of Hayashi, Takenaka et al., and Levy et al., taken alone or in combination, teach or suggest administering dried Dunaliella algae comprising β-carotene to a subject, as claimed in newly added claim 28.

As discussed above, Hayashi does not teach or suggest administering dried Dunaliella algae comprising β-carotene to a subject, as recited in newly added claim 28. Applicants submit that Takenaka et al. and Levy et al., taken alone or in combination, do not cure the deficiencies of Hayashi. Please see the above discussions of Hayashi, Takenaka et al., and Levy et al.

None of Beck, Pan et al., Heyman et al., and Smith, taken alone or in combination, cures the deficiencies of Hayashi, Takenaka et al., and Levy et al., because none of Beck, Pan et al., Heyman et al., and Smith, teach or suggest a method for reducing insulin and/or glucose plasma levels in a subject afflicted with diabetes by administering dried Dunaliella algae comprising β -carotene to the subject thereby reducing the subject's plasma insulin and/or glucose plasma levels, as claimed in newly added claim 28.

In view of the foregoing, assuming *arguendo* that Hayashi constitutes prior art, it is submitted that nothing in any of the applied references, taken alone or in combination, renders the claimed invention obvious within the meaning of 35 USC § 103.

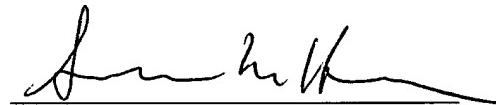
Conclusion

In view of the foregoing, Applicant submits that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicant petitions for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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